

need to recognize RLS early, even in Asian populations where RLS is apparently rare so that appropriate effective treatment can be instituted. Further studies into the pathophysiological link between RLS and SCA3 would be of academic interest.

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### Does Aripiprazole Have a Role in Treating Cognitive Impairment in Parkinson's Disease?

*SIR:* Case reports of aripiprazole treating psychosis in Parkinson's disease have been reported.<sup>1</sup> We present a case in which aripiprazole, an atypical antipsychotic with 5HT<sub>2A</sub> antagonist, 5HT<sub>1A</sub> partial agonist activity, improved cognitive functioning in a 57-year-old veteran

with a recent diagnosis of Parkinson's disease and depression.<sup>2</sup>

#### Case Report

The patient had marked cognitive impairment confirmed by neuropsychiatric testing, indicating slowing in processing information (bradyphrenia), with learning and memory deficits. The patient presented to scheduled appointments along with a social worker because of difficulty in expressing himself. Medications comprised paxil, 20mg, and his antiparkinsons medications (sinemet and artane). He continued to do poorly in the subsequent months, with increasing episodes of confusion, depression, apathy, social isolation, and decline in working memory. Residential care was being considered. After several failed attempts in adjusting medications, the patient was started on a regimen of aripiprazole, 5 mg and increased to 15 mg, in the hopes of improving cognition. When the patient presented subsequently for his appointment, he showed marked signs of cognitive improvement. His memory, mood, verbal fluency, processing speed, alertness, and interaction dramatically improved. In the past, he was unable to drive a vehicle but since being on aripiprazole, he has been driving his vehicle with no further episodes of confusion. He continues to do well on aripiprazole.

#### Comment

Early cognitive impairment with five times the risk of developing dementia is noted in Parkinson's patients due to dopamine and cholinergic deficits in the prefrontal cortex<sup>3,4</sup> with frontal and hippocampal atrophy noted in imaging studies of nondemented Parkinson's patients.<sup>3</sup> Rivastigmine was shown to improve cognitive slowing in Parkinson's disease, suggesting acetylcholine is involved in processing information speed.<sup>3</sup>

Aripiprazole partial agonist action on 5HT<sub>1A</sub> may increase cortical acetylcholine release, improving cognition.<sup>5</sup> Loss of pigmented neurons in the ventral tegmental area in a small group of patients with Parkinson's disease have been reported.<sup>3</sup> Systemic administration of the 5-HT<sub>2A</sub> receptor antagonist enhances activity of midbrain dopamine neurons, increasing dopamine in the prefrontal cortex.<sup>6,7</sup> 5HT<sub>1A</sub> and 5HT<sub>2A</sub> receptors are located primarily on the pyramidal cortical neurons (5HT<sub>2A</sub> receptors excitatory and 5HT<sub>1A</sub> receptors inhibitory), mediating a physiological balance between excitatory and inhibitory inputs onto prefrontal pyramidal neurons.<sup>2</sup> Aripiprazole's unique actions on D<sub>2</sub> receptors possibly depend upon the cellular milieu of D<sub>2</sub> receptors (receptor and G protein complement and concentration) eliciting agonist, antagonist, partial agonist activity,<sup>2</sup> which may enhance cognitive function. The most common psychiatric disturbance in Parkinson's disease is depression with a frequency of approximately 40%, occurring usually in the early and late stages of the disease.<sup>4,8</sup> A significant correlation exists between cognitive deficits and severity of depression.<sup>4</sup> Depression and dementia, not motor symptoms, were associated with increased mortality in Parkinson's disease.<sup>2</sup> Aripiprazole is a unique atypical which may have a role in improving mood and cognition in Parkinson's disease.

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